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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,647	03/01/2002	Jan Van der Greef	101137-32	7306

7590 08/22/2005

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EXAMINER

LUM, LEON YUN BON

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/980,647

Applicant(s)

VAN DER GREEF ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed 09 June 2005 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In claim 2, lines 7-9, the phrase "the dissociation step is a low pH stock, contacting with a high ionic strength solution, contacting with an organic solvent and contact with a chaotropic reagent" is vague and indefinite. Is the list of dissociation types a Markush group or does the dissociation step actually include each of the dissociation types? Since the specification does not indicate that the dissociation step requires each of the different dissociation types, the Examiner interprets the phrase to be an improper Markush group.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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8. Claims 1 and 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterkamp et al (Analytical Chemistry, 1994, vol. 66, pages 4295-4301) in view of Hsieh et al (Molecular Diversity, 1996, vol. 2, pages 189-196).

Oosterkamp et al reference teaches a method wherein in a first step, affinity proteins such as antibodies or avidin (i.e. known amount of affinity molecules) are added to an LC effluent (i.e. effluent of fractionation step) to react with ligands eluting from the LC column and that in a second step, unbound affinity proteins react with an excess of labeled ligand (i.e. known amount of a known ligand capable of binding to affinity molecule) to titrate the remaining free binding sites, wherein prior to detection of the labeled ligand/protein complex (i.e. detection of bound known ligands), free and bound label are separated (i.e. separation step to separate free and bound known ligands). See page 4295, abstract, lines 1-11.

However, Oosterkamp et al reference fails to teach the on-line coupling of the effluent of the fractionation to a mass spectrometer, wherein detection of either the free or bound known ligands is performed using the mass spectrometer.

Hsieh et al reference discloses combining chromatography with mass spectrometry to identify binders which interact with target biomolecules and study receptor-ligand interactions, in order to reduce the time for screening, ligand purification, characterization and identification, and maximizes the amount of information related to the ligand in a single experiment. See page 191, left column, 1st paragraph, lines 1-18.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Oosterkamp et al, with the step of combining

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chromatography with mass spectrometry to identify binders which interact with target biomolecules and study receptor-ligand interactions, as taught by Hsieh et al, in order to reduce the time for screening, ligand purification, characterization and identification, and maximizes the amount of information related to the ligand in a single experiment. The on-line coupling of mass spectrometry, as taught by Hsieh et al, provides the advantage of more efficient and effective characterization and identification of the ligand/protein complex of Oosterkamp et al. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in detecting binders and receptor-ligand interactions using mass spectrometry, as taught by Hsieh et al, in the method of Oosterkamp et al, since Oosterkamp et al teach chromatographic separation of complexed analytes, and the mass spectrometry taught by Hsieh et al can be coupled with chromatographic separations and is able to detect biomolecule interactions.

With regards to claim 5, Hsieh et al teach that chromatography is combined with size exclusion separation (i.e. removes high molecular weight background). See page 191, left column, 1st paragraph.

With regards to claim 6, Oosterkamp et al teach an HPLC column. See Figure 1 and caption.

With regards to claim 7, Hsieh et al teach that analyses are performed by matrix-assisted laser desorption/ionization time-of-flight. See page 195, left column, 1st paragraph.

With regards to claim 8, Hsieh et al that with ESI mass spectrometry, the mass range for protein targets is 500-3000 m/z. See page 195, left column, 1st full paragraph, lines 1-2.

With regards to claim 9, Hsieh et al teach a library of components and results from mass spectrometry (i.e. compound detected). See Table 1 and caption; and Figure 4 and caption.

9. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterkamp et al (Analytical Chemistry, 1994, vol. 66, pages 4295-4301) in view of Hsieh et al (Molecular Diversity, 1996, vol. 2, pages 189-196) as applied to claim 1 above, and further in view of Jurinke et al (US 6,303,309 B1) and Lutz et al (Journal of Chromatography, 1996, vol. 755, pages 179-187).

Oosterkamp et al and Hsieh et al references have been disclosed above and Oosterkamp et al additionally teach a restricted-access reversed-phase support was placed in the carrier stream prior to the detector, wherein free fluorescein-biotin is retained at the hydrophobic inner surface of the pores and the avidin/biotin and avidin/fluorescein-biotin complexes are excluded from the pores and pass unretained to the detector (i.e. separation step comprises the retention of the free ligand from the effluent using a restricted-access support, whereby the ligand-affinity molecule complex is permeated). See page 4298, left column, 1st full paragraph; and Figure 1 and caption. However, Oosterkamp et al and Hsieh et al fail to teach that the bound ligands are detected after being separated from said ligand-affinity molecule complex in a

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dissociation step, followed by separation of the ligand from the affinity molecule using a hollow-fiber module, and directing the permeate stream containing the ligand to the mass spectrometer, in which method the dissociation step is preferably contacting with a high ionic strength solution.

Jurinke et al reference teaches decomplexation of biotin and biotin-binding compounds (i.e. separation) using ammonia, such as ammonium salt (i.e. high ionic strength solution), in order to isolate biotin compounds for analysis using mass spectrometry, wherein biotin-binding compounds include avidin. See column 3, lines 1-3; column 3, line 66 to column 4, line 7; column 5, lines 23-29; and column 6, lines 46-63.

Lutz et al reference teaches introducing a membrane into the system with a cut-off between the size of a large antibody and a label so that free label passes the membrane freely, whereas the antibody-bound label will remain in the retentate stream and the permeate stream with free label is sent for detection, wherein separation of free and antibody-bound antigen is performed on a hollow-fibre module, and wherein free label is a labeled biotin, in order to perform a separation based solely on size and does not require regeneration. See page 181, left column, 2nd full paragraph ; page 182, left column 1st paragraph, lines 3-9; page 182, right column, 1st full paragraph, lines 1-6; page 187, left column, 1st paragraph, lines 3-5; and Figures 2-3 and captions.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Oosterkamp et al and Hsieh et al references with decomplexation of biotin and biotin-binding compounds using ammonia, such as

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ammonium salt, as taught by Jurinke et al, in order to isolate biotin compounds for analysis using mass spectrometry. The decomplexation of biotin and biotin-binding compounds using ammonia, as taught by Jurinke et al, provides the advantage of separating certain compounds for use in the mass spectrometry of Oosterkamp et al and Hsieh et al. In addition, one of ordinary skill in the art at the time of the invention would have reasonable expectation of success in decomplexing biotin and biotin-binding compounds using ammonia, as taught by Jurinke et al, in the methods of Oosterkamp et al and Hsieh et al, since Oosterkamp et al and Hsieh et al teach the complexing of avidin affinity proteins to unlabelled and labeled biotin analytes for the detection of biotin using mass spectrometry, and the decomplexation taught by Jurinke et al is performed on avidin-biotin complexes for the purpose of mass spectrometry.

It would also have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Oosterkamp et al and Hsieh et al introducing a membrane into the system with a cut-off between the size of a large antibody and a label so that free label passes the membrane freely, whereas the antibody-bound label will remain in the retentate stream and the permeate stream with free label is sent for detection, wherein separation of free and antibody-bound antigen is performed on a hollow-fibre module, and wherein free label is a labeled biotin, as taught by Lutz et al, in order to perform a separation based solely on size and does not require regeneration. The hollow-fibre module of Lutz et al provides the advantage of further separating and purifying biomolecules without requiring regeneration for the method of Oosterkamp et al and Hsieh et al. Furthermore, one of ordinary skill in the art at the time of the

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invention would have reasonable expectation of success in applying hollow membrane fiber separation, as taught by Lutz et al, in the method of Oosterkamp et al and Hsieh et al, since Oosterkamp et al and Hsieh et al references teach the detection of biotin analytes, and the hollow fiber membrane, which retains larger particles, would retain bound complexes and allow smaller, labeled biotin to pass through to the detector. Since Jurinke et al reference teaches the decomplexation of avidin and biotin, the hollow fiber membrane would retain the larger avidin molecule and allow the permeation of biotin to the detector.

10. Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterkamp et al (Analytical Chemistry, 1994, vol. 66, pages 4295-4301) in view of Hsieh et al (Molecular Diversity, 1996, vol. 2, pages 189-196) as applied to claim 1 above, and further in view of Lutz et al (Journal of Chromatography, 1996, vol. 755, pages 179-187).

Oosterkamp et al reference and Hsieh et al references have been disclosed above and Oosterkamp et al reference additionally teaches that a restricted-access reversed-phase support was placed in the carrier stream prior to the detector, wherein free fluorescein-biotin is retained at the hydrophobic inner surface of the pores and avidin/biotin and avidin/fluorescein-biotin complexes are excluded from the pores and pass unretained to the detector, and wherein after free fluorescein-biotin was retained on the support, the column was easily regenerated by rinsing with acetonitrile:water (i.e. the separation step comprises the retention of the free ligand from the effluent using a

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restricted-access support, whereby the ligand-affinity molecule complex is permeated, followed by the elution of the unbounded ligands from the restricted-access support using a suitable carrier stream). See (page 4298, left column, 1st full paragraph; page 4298, right column, 2nd paragraph; and Figure 1 and caption). However, Oosterkamp et al and Hsieh et al fail to that the separation step comprises the retention of the ligand-affinity molecule complex from the effluent using a hollow-fiber module, whereby the free ligand is permeated, and the permeate stream with the free ligand is subsequently directed to the mass spectrometer (claim 3), and fails to teach the step of directing the eluted stream containing the free ligand to the mass spectrometer (claim 4).

Lutz et al reference teaches introducing a membrane into the system with a cut-off between the size of a large antibody and a label so that free label passes the membrane freely, whereas the antibody-bound label will remain in the retentate stream and the permeate stream with free label is sent for detection, wherein separation of free and antibody-bound antigen is performed on a hollow-fibre module, and wherein free label is a labeled biotin, in order to perform a separation based solely on size and does not require regeneration. See page 181, left column, 2nd full paragraph ; page 182, left column 1st paragraph, lines 3-9; page 182, right column, 1st full paragraph, lines 1-6; page 187, left column, 1st paragraph, lines 3-5; and Figures 2-3 and captions.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Oosterkamp et al and Hsieh et al introducing a membrane into the system with a cut-off between the size of a large antibody and a label so that free label passes the membrane freely, whereas the antibody-bound label

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will remain in the retentate stream and the permeate stream with free label is sent for detection, wherein separation of free and antibody-bound antigen is performed on a hollow-fibre module, and wherein free label is a labeled biotin, as taught by Lutz et al, in order to perform a separation based solely on size and does not require regeneration. The hollow-fibre module of Lutz et al provides the advantage of further separating and purifying biomolecules without requiring regeneration for the method of Oosterkamp et al and Hsieh et al. In addition, one of ordinary skill in the art at the time of the invention would have reasonable expectation of success in applying hollow membrane fiber separation, as taught by Lutz et al, in the method of Oosterkamp et al and Hsieh et al, since Oosterkamp et al and Hsieh et al references teach the detection of biotin analytes, and the hollow fiber membrane, which retains larger particles, would retain bound complexes and allow smaller, labeled biotin to pass through to the detector. Since Jurinke et al reference teaches the decomplexation of avidin and biotin, the hollow fiber membrane would retain the larger avidin molecule and allow the permeation of biotin to the detector.

With regards to claim 4, Lutz et al reference also discloses a permeate stream only containing free label and a retentate stream consisting bound label, in order to provide both free and antibody-bound label in separate streams that can be used for quantifying the original analyte concentration. See page 182, right column, 1st full paragraph, lines 1-6; and Figure 3 and caption.

Response to Arguments

11. Due to the amendments to claims 1-5 and 7, as stated on page 5 of the Remarks, filed 09 June 2005, the claim objections and rejections made under 35 U.S.C. 112, 2nd paragraph in the previous Office Action have been overcome.

12. On page 6 of the Remarks, Applicants argue that there is no motivation to combine Oosterkamp et al with the teaching of Hsieh et al since Hsieh et al is hampered by background signals. Specifically, Applicants mention that Hsieh's method requires a dual run, a first run in absence of a target library and a second run in the presence of the library, which indicates that background compounds are always present in the assay and would limit the efficiency, selectivity, and flexibility of the method.

Applicant's arguments have been fully considered, but are not persuasive. The mere fact that Hsieh's method applies the dual run is to cancel out the presence of any background signals, thereby rendering any interference from background components moot. The methodology of Hsieh et al is therefore not hampered by the background signals since the methodology teaches a way to overcome the signals. In addition, the previous Office Action provided proper motivation as well as a reasonable expectation of success for combining the methodology of Hsieh et al with Oosterkamp et al. Hsieh et al teach that mass spectrometry is one type of detection step that can be combined with the type of chromatographic separations taught by Oosterkamp et al, and has the advantages of reducing the time required for screening, ligand purification,

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characterization and identification, and also maximizes the amount of information related to the ligand in a single experiment. Therefore, Hsieh et al do not in fact teach away from the claimed invention and provides proper motivation to combine with the teachings of Oosterkamp et al. Applicant's arguments are therefore not persuasive and the rejection made in the previous Office Action is maintained.

13. On page 7 of the Remarks, Applicants argue that there is no suggestion in Jurinke et al that would lead the skilled person to the idea that the dissociation would be suitable in an on-line method, which requires a relative fast reaction time, preferably under ambient conditions and preferably without a need to remove the ammonia, and that the conditions disclosed in Jurinke et al are typically off-line conditions instead of on-line conditions.

Applicant's arguments have been fully considered, but are not persuasive. Applicants contend that a suitable on-line method requires a "**relative** fast reaction time, **preferably** under ambient conditions and **preferably** without a need to remove the ammonia", and that the conditions disclosed in Jurinke et al are "typically off-line conditions" (see page 7, 2nd paragraph). By stating that the reaction time, ambient conditions, and ammonia removal are only preferred conditions used in on-line applications, Applicant's argument does not exclude the possibility of having the conditions disclosed by Jurinke et al in an on-line application. Applicants have also not cited the specification or evidence otherwise to support the claim that the stated

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conditions are in fact on-line conditions, and that the conditions disclosed in Jurinke et al cannot be applied to on-line applications.

The previous Office Action, however, provides sufficient motivation and reasonable expectation of success in combining the method of Jurinke et al with Oosterkamp et al and Hsieh et al. By disclosing that ammonia can be used to isolate biotin compounds for mass spectrometry, Jurinke et al teaches a dissociation method that can be applied to both a compound (biotin) and method of detection (mass spectrometry) that are compatible with the teachings of Oosterkamp et al and Hsieh et al. In addition, Oosterkamp et al and Hsieh et al teach the detection of analytes after a separation step, and the dissociation step of Jurinke et al is one type of separation step.

Therefore, Applicant's arguments are not considered to be persuasive and the rejection set forth in the previous Office Action is maintained.

14. On pages 7-8 of the Remarks, Applicants argue that the skilled person would have no reason to use the hollow fibre membrane taught by Lutz et al with any of the other applied references since the hollow fibre membrane of Lutz et al is used to separate free and bound labels for fluorescence detection whereas in the instant invention, mass spectrometry is applied to detect the ligand also in the presence of the affinity molecule. Applicants conclude by stating that the hollow fiber module is used for a completely different reason.

Applicant's arguments have been fully considered, but are not persuasive. Applicants compared the detection systems of the applied references and the instant

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application as a reason for why Lutz et al does not apply. However, Lutz et al is only applied to teach the hollow fibre membrane and not the detection method, which has already been applied by Hsieh et al as a mass spectrometer. As stated in the previous Office Action, Lutz et al provides proper motivation and a reasonable expectation of success for combining the hollow fibre membrane with the method of Oosterkamp et al and Hsieh et al since the membrane provides the advantage of separating solely upon size and does not require regeneration, and the membrane would be able to separate the bound complexes taught by Oosterkamp et al and Hsieh et al. Furthermore, although Applicants state that the hollow fiber module in the instant application is used for a different reason than that of Lutz et al, since Applicants do not provide a further statement on the issue and since the claimed invention only states "separation of the ligand from the affinity molecule using a hollow-fiber module", Applicant's statement is not considered to be persuasive.

Therefore, Applicant's arguments are not found to be convincing and the rejection set forth in the previous Office Action is maintained.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/516,441. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons:

Claims 1-9 of the instant application recite an on-line detection method comprising the on-line coupling of an effluent of a fractionation step to a mass spectrometer, in which the method comprises the addition of a known amount of affinity molecules to the effluent of the fractionation step, whereby the affinity molecules bind analytes in the effluent, followed by the addition of a known amount of a known ligand capable of binding to the affinity molecule under suitable binding conditions, followed by a separation step to separate free and bound known ligands and finally detection of either the free or bound known ligands using the mass spectrometer.

Claims 1-12 of the copending application teach each and every limitation of the instant invention, wherein the enzyme is the affinity molecule, the substrate is the ligand, and the step using the hollow-fibre module is the separation step.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

17. No claims are allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum
Patent Examiner
Art Unit 1641



LYL



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08/12/05